

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE**

**10th JOINT MEETING
of the
BOARD OF SCIENTIFIC ADVISORS AND
NATIONAL CANCER ADVISORY BOARD**

**Summary of Meeting
November 29, 2017**

**National Cancer Institute
Shady Grove Campus
National Institutes of Health
Bethesda, Maryland**

**BOARD OF SCIENTIFIC ADVISORS and
NATIONAL CANCER ADVISORY BOARD
BETHESDA, MARYLAND
Summary of Meeting
November 29, 2017**

The Board of Scientific Advisors (BSA) and the National Cancer Advisory Board (NCAB) convened for the 10th Joint Meeting on 29 November 2017, in Conference Room TE406, East Wing, Shady Grove Campus, National Cancer Institute, National Institutes of Health (NIH), Bethesda, MD. The meeting was open to the public on Wednesday, 29 November 2017, from 8:30 a.m. to 4:01 p.m., and closed to the public Wednesday, 29 November 2017, from 4:15 p.m. to 5:00 p.m. The NCAB Chair, Dr. Elizabeth M. Jaffee, Deputy Director, The Sidney Kimmel Comprehensive Cancer Center, Co-Director, Skip Viragh Center for Pancreas Cancer, The Dana and Albert “Cubby” Broccoli Professor of Oncology, Johns Hopkins University, and the BSA Chair, Dr. Chi V. Dang, Scientific Director, Ludwig Institute for Cancer Research, Professor, The Wistar Institute, presided during the open session. Dr. Jaffee presided during the closed session.

BSA Members

Dr. Chi V. Dang (Chair)
Dr. Kenneth C. Anderson
Dr. Dafna Bar-Sagi
Dr. Ethan M. Basch
Dr. Michael John Becich
Dr. Sangeeta N. Bhatia
Dr. Melissa L. Bondy (absent)
Dr. Arul M. Chinnaiyan (absent)
Dr. Graham A. Colditz
Dr. Christopher M. Counter
Dr. Joseph M. DeSimone (absent)
Dr. Daniel C. DiMaio
Dr. Karen M. Emmons
Dr. Carol E. Ferrans
Dr. Chanita A. Hughes-Halbert (absent)
Dr. James V. Lacey
Dr. Maria Elena Martinez
Dr. Luis F. Parada (absent)
Dr. Sylvia Katina Plevritis
Ms. Diane Zipursky Quale
Dr. Martine F. Roussel
Dr. Robert D. Schreiber
Dr. Victoria L. Seewaldt
Dr. Kevin M. Shannon (absent)
Ms. Mary L. Smith
Dr. Ian M. Thompson, Jr.
Dr. David A. Tuveson
Dr. Cheryl L. Walker
Dr. Eileen P. White
Dr. Kevin P. White
Dr. Cheryl L. Willman (absent)

NCAB Members

Dr. Elizabeth M. Jaffee (Chair)
Dr. Peter C. Adamson
Dr. Francis Ali-Osman
Dr. Deborah Watkins Bruner
Dr. Yuan Chang (Absent)
Dr. David C. Christiani
Dr. Judy E. Garber
Mr. Lawrence O. Gostin (absent)
Dr. Scott W. Hiebert
Dr. Beth Y. Karlan
Dr. Timothy J. Ley
Dr. Electra D. Paskett
Dr. Nancy J. Raab-Traub (absent)
Dr. Mack Roach III
Dr. Charles L. Sawyers (absent)
Dr. Margaret R. Spitz
Dr. Max S. Wicha

Alternate Ex Officio NCAB Members

Dr. Robert T. Anderson, DOE (absent)
Dr. Michael A. Babich, CPSC
Dr. Vincent J. Cogliano, EPA (absent)
Dr. Michael Kelley, VA (absent)
Dr. Aubrey Miller, NIEHS (absent)
Dr. Richard Pazdur, FDA (absent)
Dr. Craig D. Shriver, DoD
Dr. Kerry Souza, NIOSH (absent)
Dr. Lawrence A. Tabak, NIH (absent)
Dr. Richard J. Thomas, DOL

Members, Scientific Program Leaders, National Cancer Institute, NIH

Dr. Norman E. Sharpless, Director, National Cancer Institute
Dr. Jeff Abrams, Acting Director for Clinical Research, Division of Cancer Treatment and Diagnosis
Dr. L. Michelle Bennett, Director, Center for Research Strategy
Dr. Stephen J. Chanock, Director, Division of Cancer Epidemiology and Genetics
Dr. Henry P. Ciolino, Director, Office of Cancer Centers
Dr. Robert Croyle, Director, Division of Cancer Control and Population Sciences
Dr. William Dahut, Scientific Director for Clinical Research, Center for Cancer Research
Dr. James H. Doroshow, Deputy Director for Clinical and Translational Research
Dr. Dan Gallahan, Deputy Director, Division of Cancer Biology
Dr. Paulette S. Gray, Director, Division of Extramural Activities
Dr. Ed Harlow, Special Advisor to the Director
Dr. Toby T. Hecht, Deputy Director, Division of Cancer Treatment and Diagnosis
Dr. Tony Kerlavage, Acting Director, Center for Biomedical Informatics and Information
Technology
Dr. Kristin Komschlies, Acting Director, Office of Scientific Operations, NCI Campus at Frederick
Dr. Barry Kramer, Director, Division of Cancer Prevention
Dr. Jerry Lee, Deputy Director, Center for Strategic Scientific Initiatives
Dr. Douglas R. Lowy, Deputy Director, National Cancer Institute
Dr. Glenn Merlino, Scientific Director for Basic Research, Center for Cancer Research
Dr. Tom Misteli, Director, Center for Cancer Research
Ms. Donna Siegle, Acting Executive Officer, and Acting Deputy Director for Management
Dr. Dinah Singer, Acting Deputy Director and Director, Division of Cancer Biology
Dr. Sanya Springfield, Director, Center to Reduce Cancer Health Disparities
Dr. Louis M. Staudt, Director, Center for Cancer Genomics
Dr. Ted Trimble, Director, Center for Global Health
Mr. Michael Weingarten, Director, Small Business Innovation Research and Small Business Technology
Transfer Programs
Dr. Jonathan Wiest, Director, Center for Cancer Training
Dr. Robert Yarchoan, Director, Office of HIV and AIDS Malignancy
Dr. Maureen Johnson, Executive Secretary, Office of the Director

Liaison Representatives

Ms. Carolyn Aldige, Prevent Cancer Foundation
Ms. Paula Bowen, Kidney Cancer Association
Mr. William Bro, Kidney Cancer Association
Dr. Carol Brown, Society of Gynecologic Oncologists
Dr. Margaret Foti, American Association for Cancer Research
Dr. Leo Giambaresi, American Urological Association
Dr. Francis Giardiello, American Gastroenterological Association
Dr. Mary Gullatte, Oncology Nursing Society
Dr. Ruth Hoffman, American Childhood Cancer Organization
Dr. Gerald F. Joseph, American College of Obstetricians and Gynecologists
Dr. Steven L. Klein, National Science Foundation
Ms. Laura Levit, American Society of Clinical Oncology
Dr. W. Marston Linehan, Society of Urologic Oncology
Ms. Margo Michaels, Education Network to Advance Cancer Clinical Trials
Dr. Patricia Mullan, American Association for Cancer Education
Ms. Shelly Fuld Nasso, National Cancer Institute, Council of Research Advocates

Ms. Leah Ralph, Association of Community Cancer Centers
Ms. Susan Silver, National Coalition for Cancer Survivorship
Ms. Christy Schmidt, American Cancer Society
Ms. Barbara Duffy Stewart, Association of American Cancer Institutes
Dr. Johannes Vieweg, American Urological Association
Dr. Pamela A. Wilcox, American College of Radiology
COL (Ret.) James E. Williams, Jr., Intercultural Cancer Council

TABLE OF CONTENTS

WEDNESDAY, 29 NOVEMBER 2017

I.	Call to Order and Opening Remarks—Drs. Chi V. Dang and Elizabeth M. Jaffee.....	1
II.	Future Board Meeting Dates—Drs. Chi V. Dang and Elizabeth M. Jaffee.....	1
III.	NCI Director’s Report—Dr. Norman E. Sharpless.....	1
	Questions and Answers.....	4
IV.	Legislative Report—Ms. M. K. Holohan.....	5
V.	Presidents’ Cancer Panel Report—Dr. Barbara K. Rimer.....	6
	Questions and Answers.....	7
VI.	Recognition of Retiring BSA Members—Dr. Norman E. Sharpless.....	8
VII.	High-Quality Risk-Based Cervical Cancer Screening for the United States and the World— Drs. Mark C. Schiffman and Nicolas Wentzensen.....	8
	Questions and Answers.....	10
VIII.	Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE™)—Drs. Paul Jacobsen, Sandra A. Mitchell, and Lori Minasian.....	11
	Questions and Answers.....	13
IX.	Early Career Investigators and NCI Planning—Dr. L. Michelle Bennett.....	14
	Questions and Answers.....	15
X.	RFA/Cooperative Agreement Concepts (Coop. Agr.)—New and Re-Issue—NCI Staff.....	16
	Office of the Director	
	Investigation of the Transmission of Kaposi Sarcoma-Associated Herpesvirus (KSHV)—Dr. Rebecca Liddell Huppi.....	16
	SBIR Phase IIB Bridge Awards to Accelerate the Development of Cancer-Focused Technologies Toward Commercialization—Dr. Todd Haim.....	17
	Division of Cancer Prevention	
	NCI Community Oncology Research Program—Dr. Wortia McCaskill-Stevens.....	18
	Office of the Director	
	AIDS and Cancer Specimen Resource (ACSR)—Dr. Rebecca Liddell Huppi.....	19
XI.	Subcommittee Reports—Dr. Elizabeth M. Jaffee.....	20
	NCAB <i>ad hoc</i> Subcommittee on Global Cancer Research—Dr. Francis Ali-Osman.....	20
	NCAB <i>ad hoc</i> Subcommittee on Population Science, Epidemiology, and Disparities—Dr. Electra D. Paskett.....	21
	BSA <i>ad hoc</i> Subcommittee on HIV and AIDS Malignancy—Dr. Robert Yarchoan.....	21
XII.	Ongoing and New Business—Drs. Chi V. Dang and Elizabeth M. Jaffee.....	21
	Establishing BSA and NCAB Working Groups.....	21
XIII.	NCAB Closed Session—Dr. Elizabeth M. Jaffee.....	22
XIV.	Adjournment—Drs. Chi V. Dang and Elizabeth M. Jaffee.....	22

WEDNESDAY, 29 NOVEMBER 2017

I. CALL TO ORDER AND OPENING REMARKS—DRS. CHI V. DANG AND ELIZABETH M. JAFFEE

Dr. Elizabeth Jaffee called to order the 10th Joint Board of Scientific Advisors (BSA) and National Cancer Advisory Board (NCAB) meeting and welcomed members of the Board, *ex officio* members, liaison representatives, staff, and guests. Members of the public were welcomed and invited to submit to Dr. Paulette S. Gray, Director, Division of Extramural Activities (DEA), National Cancer Institute (NCI), in writing and within 10 days, any comments regarding items discussed during the meeting. Drs. Dang and Jaffee reviewed the confidentiality and conflict-of-interest practices required of Board members in their deliberations.

Motion. A motion to approve the minutes of the 12 September 2017 NCAB meeting was approved unanimously.

II. FUTURE BOARD MEETING DATES—DRS. CHI V. DANG AND ELIZABETH M. JAFFEE

Dr. Jaffee called Board members' attention to future meeting dates. She noted the following changes: the NCAB fall 2018 meeting, usually held in September, has been moved to 14–15 August 2018 to facilitate the Cancer MoonshotSM awards process; the NCAB September 2019 meeting has been rescheduled for 3–5 September 2019 to avoid conflicting with the Labor Day holiday.

Motion. A motion to confirm the 14–15 August 2018 and 3–5 September 2019 meeting dates of the NCAB was approved unanimously.

III. NCI DIRECTOR'S REPORT—DR. NORMAN E. SHARPLESS

Dr. Norman Sharpless, Director, NCI, welcomed BSA and NCAB members and attendees to the 10th joint meeting of these boards. He expressed appreciation to the meeting organizers and members for their continued support. Dr. Sharpless provided an update on NCI's budget and activities. He remarked on the organizational structure, scale, and scope of work of the NCI and the cadre of assets available to researchers. Dr. Sharpless informed members that he is continuing a listening tour of NCI's operations to crystallize new ideas and a forward vision for the Institute, which he will share with NCI staff in a Town Hall Meeting on 11 December 2017.

Dr. Sharpless expressed condolences to the family and colleagues of longtime NCAB member, Dr. Donald Coffey, on his recent passing. Dr. Coffey had been a legend in prostate cancer research and a faculty member at John Hopkins University.

Dr. Sharpless was joined by Drs. Doug R. Lowy, Deputy Director, NCI, who updated the Boards on the NCI Genomic Data Commons and physician and clinician-scientist awards; James H. Doroshow, Deputy Director, Clinical and Translational Research, NCI, who provided an update on NCI's clinical and translational activities; and Dinah Singer, Acting Deputy Director, NCI, who updated the attendees on the Cancer MoonshotSM Initiative. He expressed appreciation to Dr. Lowy for his leadership as NCI's Acting Director from 2015 to 2017.

NCI Budget. Dr. Sharpless reported that the President's fiscal year (FY) 2018 proposed budget includes a 20 percent decrease in the NIH budget, which is a substantial reduction to the FY 2017 enacted budget. Prior NIH budget allowances from the House and Senate Appropriations Subcommittees on

Labor, Health and Human Services, Education, and Related Agencies have closely aligned with enacted budgets. In fact, the House and Senate advanced their bills out of committee with FY 2018 allowances that reflect the FY 2017 enacted budget. Although the appropriations to the NIH and NCI have increased for the past 3 consecutive years, it is difficult to predict this year's outcome. Aside from NCI's regular appropriations, the Cancer MoonshotSM funding is a welcomed addition and reflects the ongoing congressional bipartisan support.

Dr. Sharpless remarked that despite the increases in regular appropriations and the number of grants awarded by the NCI during FYs 2013–2017, the success rate of competing Research Project Grant applications (RPGs or R01s) has continually decreased because of the increasing ratio of applications received to grants funded. He reported that the NCI is operating under a continuing resolution (CR) that funds the government through December 8, 2017. If the CR is extended, the trend in R01s is expected to decrease further in FY 2018. If the Senate and House budget allowances move forward, the decline in R01 success rates would be less dramatic. The enthusiasm for the Cancer MoonshotSM Initiative and the funding opportunity announcements (FOAs) have galvanized the research community for FY 2017, but they do not reflect a change or shift in the ratio of applications received/funded, in general. The NCI will be fiscally conservative when planning new opportunities to support.

NCI Activities. Dr. Sharpless reported that the NIH has broadly focused on increasing the number of Early-Stage Investigators (ESIs) through the Next Generation Research Initiative, formerly called the Grant Support Index (GSI). The NCI will present its efforts to address increasing the number ESIs later in the meeting. He introduced Dr. Ethan Dmitrovsky, the new Laboratory Director, Frederick National Laboratory for Cancer Research (FNLCR), and President, Leidos Biomedical Research, Inc., (Leidos). Dr. Sharpless expressed appreciation to Dr. David C. Heimbrook for his leadership of the FNLCR for the past 6 years.

Dr. Sharpless stated that early discussions with NCI Advisory Boards suggest a desire for increased opportunities for participating in NCI activities. He identified three areas in which the extramural community could assist the NCI: (1) investigating strategies to improve patient occupancy in the NIH Clinical Center (CC); (2) establishing new NCI Working Groups; and (3) developing scientific challenge awards that address the NCI cancer research portfolio.

NCI Genomic Data Commons (GDC). Dr. Lowy provided an update on the GDC and acknowledged the members of the GDC team. As a joint effort between the NCI, The University of Chicago, Ontario Institute for Cancer Research, and Leidos, the GDC is composed of four components: (1) System 1, data exploration and visualization portal; (2) System 2, data submission portal; (3) System 3, data harmonization; and (4) System 4, a Representational State Transfer (REST) application programming interface (API). The REST API drives the GDC data portal and data submission system and allows researchers, including third-party software programmers, to develop applications. Emphasizing the significant use of the database, he noted that in October 2017 alone, the GDC was accessed by 22,000 users who downloaded more than 2.3 petabytes of information.

Dr. Lowy informed members that in addition to the initial data sets from The Cancer Genome Atlas (TCGA) and the Therapeutically Applicable Research to Generate Effective Treatments (TARGET) project, other data sets are being deposited into the GDC. Foundation Medicine Inc. (FMI) released 18,000 genomic profiles, and the American Association of Cancer Research (AACR) project Genomics, Evidence, Neoplasia, Information, Exchange (GENIE) will, over the next 18 months, release 32,000 cases of genomic information. Furthermore, the NCI is in discussions with Palmetto Government Business Administrators, a Medicare contract organization, regarding open access to genomic and clinical data to aid in developing evidence-based genomic profiling for clinical treatment. Overall, the GDC is being

utilized to prompt change in the standard of care and reimbursements regarding genomic medicine and cancer management.

Physician and Clinical Scientists Awards. Dr. Lowy reported that the NCI has expanded the criteria and increased support for the NCI Mentored Clinical Scientist Research Career Development Award (K08) and discontinued the NCI Mentored Patient-Oriented Research Career Development Award (K23). These changes will increase the range of qualifying physician-scientist applications; increase salary levels for 100 percent time commitment to \$185,000, which can be prorated accordingly; and increase research support for successful applications to \$50,000 per year.

Dr. Lowy called attention to the Lasker Scholars Program, which is an intramural and extramural partnership to provide clinical investigators an opportunity to begin an independent research career at the NIH Clinical Center. Lasker Clinical Research Scholars may choose to continue at the NIH or move to an extramural sponsoring institution following completion of the initial phase. Lasker Scholars are funded for up to 10 years: 5 to 7 years at the NIH and up to an additional 3 years at an extramural institution.

Cancer MoonshotSM Initiative. Dr. Singer updated members on the implementation of the NCAB Blue Ribbon Panel (BRP) recommendations for the Cancer MoonshotSM, which are detailed in the September 2016 BRP Report. Despite a delay in funding from the time the BRP submitted its report, the NCI capitalized on highly accomplished areas of research, which had been identified as scientific opportunities to accelerate, and rapidly issued 10 Cancer MoonshotSM Requests for Applications (RFAs) in FY 2017. Most of the RFAs will establish networks of specialized research and are focused on immunotherapy (12 awards), new enabling technologies (7 awards), drug resistance (5 awards), and symptom management (6 awards). In addition to the 10 RFAs, the NCI used such approaches as partnerships, contracts, and supplements to rapidly implement the BRP recommendations. The initiatives that are being supported include the Partnership for Accelerating Cancer Therapies (PACT), Gene Fusions in Pediatric Sarcomas, Generation of a Human Tumor Atlas Pilot Program, and Smoking Cessation Program and Tobacco Control in Cancer Patients. In addition, to address the Cancer MoonshotSM Task Force agenda on interagency collaborations, NCI engaged in the following science initiatives: Applied Proteogenomics Organizational Learning and Outcomes (APOLLO) Network and the Department of Energy–NCI Predictive Modeling project.

Dr. Singer described the in-depth Cancer MoonshotSM implementation plan for FYs 2018 and 2019, which involves establishing 13 trans-NCI Cancer MoonshotSM Implementation Teams (CMITs) to develop initiatives and manage post-award operations for each of the 10 BRP recommendations. One of the CMITs also is focused on establishing public-private partnerships. The NCI issued and published 18 RFAs for FY 2018, most of which have submission deadlines in December 2017 or January 2018. In addition, intramural concepts have been launched for FY 2018, including the Rare Tumor Engagement Network.

NCI Clinical and Translational Update. Dr. Doroshow provided an overview of the PACT, a public-private partnership to promote immunotherapy biomarker development, which complements other NCI initiatives, including the Cancer Immune Monitoring and Analysis Centers (CIMACs) and the Cancer Immunologic Data Commons. After 1.5 years of discussions with representatives from the pharmaceutical industry, led by NIH director Francis S. Collins, the PACT launched in October 2017. This broader immunotherapy biomarker development effort consists of 12 pharmaceutical companies, an executive committee composed of NIH/NCI and industry partner leaderships, and joint NCI and industry partner steering committees. The PACT will double the NCI biomarker investments and development capabilities for NCI's National Clinical Trials Network (NCTN) trials and industry-sponsored trials.

Dr. Doroshow informed members that the NCI is actively engaged in establishing new agreements with pharmaceutical companies to obtain novel agents for the NCI Formulary that can be used in preclinical and clinical studies. The Formulary currently consists of nine companies that collectively have provided 27 agents. Multiple projects are at various stages of the approval process.

Dr. Doroshow reported that the second phase of the Molecular Analysis for Therapy Choice (MATCH) trial, the Rare Variant Initiative, opened during July–August 2017 following completion of the initial MATCH trial. Several academic institutions and commercial laboratories are submitting proposals to participate as NCI-MATCH laboratories, which will involve qualifying their in-house institutional next-generation sequencing (NGS) panels that will be used to refer patients with low-frequency mutations to one of the 18 study treatment arms. To date, 74 patients who were identified by already-approved outside-of-the-trial NGS providers (i.e., FMI, MD Anderson Cancer Center, or Memorial Sloan Kettering Cancer Center) have been enrolled, and 45 patients have been assigned to treatment arms. The NCI anticipates having a national approach to identify patients for Phase II precision medicine trials. Dr. Doroshow remarked that results from the first MATCH trial treatment arm that reached its accrual goals have been reported.

Questions and Answers

Ms. Mary Lou Smith, Co-founder, Research Advocacy Network, wondered whether patients were aware of the opportunity to be treated at the CC. Dr. Sharpless explained that CC patients were primarily local to the Washington, D.C., metropolitan region. Although procedures that were once unique to the CC are being performed at other NCI-designated Cancer Centers, the NCI and the cancer community can take steps to inform patients about clinical trials not being performed elsewhere.

In response to a query by Dr. Jaffee on the strength of the CC support services, Dr. Sharpless replied that as a research institution and not a full-service hospital, the CC does well in its efforts but has some limited capabilities. Dr. William D. Merritt, Program Director, Cancer Therapy Evaluation Branch (CTEP), Division of Cancer Treatment and Diagnosis (DCTD), NCI, added that cancer therapy, intensive care, consulting and imaging services, and infectious disease response are strongly supported at the CC. Obstetrics and gynecology, radiology, and operating room services are not as efficient.

Dr. Max S. Wicha, Deputy Director, Taubman Institute, Distinguished Professor of Oncology, and Professor, Internal Medicine, Division of Hematology and Oncology, University of Michigan, asked about plans to develop new chimeric antigen receptor T lymphocyte antigen targets. Dr. Sharpless explained that Dr. Steven A. Rosenberg, Chief, Surgery Branch, Cancer Center for Research (CCR), has several patients in clinical trials who are benefiting, but current production capabilities are below desired levels to meet CC's demands. Limiting factors are based on the necessary current Good Manufacturing Practice (cGMP) requirements. Efforts are ongoing to increase production capacity, and the NIH anticipates expanding production by 2020.

Dr. James V. Lacey, Jr., Director and Professor, Division of Cancer Etiology, Department of Population Sciences, Beckman Research Institute, City of Hope, suggested shifting, in the long term, from the traditional mode of data sharing to one that would accelerate the data as a “core layer” and the analytics as a “core product” in implementing the Cancer MoonshotSM recommendations. Dr. Singer explained that ongoing discussions with the Center for Biomedical Informatics and Information Technology (CBIIT) are exploring ways to integrate the many data-generating initiatives into a common platform.

Dr. Victoria L. Seewaldt, Ruth Zeigler Professor, Chair, Department of Population Sciences, Beckman Research Institute, City of Hope, asked about NCI's vision for global health and the plans to

address the NCI-designated Cancer Centers' international catchment areas. Dr. Sharpless reflected on his experiences working internationally that formulated a desire and interest for a global health agenda, which aligns with former NCI director Dr. Harold Varmus's rationale for establishing the NCI Center for Global Health (CGH). The challenge lies in prioritizing the CGH's many functions and research opportunities. Establishing a new Working Group on Global Health will begin to address this issue. Dr. Sharpless also explained that the NCI has not had discussions with NCI-designated Cancer Center directors regarding catchment areas, but a list of global research activities and resources has been compiled.

Dr. Beth Y. Karlan, Director, Women's Cancer Program, Samuel Oschin Comprehensive Cancer Institute, Director of Gynecologic Oncology, Department of Obstetrics and Gynecology, Cedar-Sinai Medical Center, and Professor, Obstetrics and Gynecology, David Geffen School of Medicine, University of California, Los Angeles, sought clarity on the 100 percent time commitment requirements of the K08 award. Dr. Lowy clarified that the requirements are not fixed at 100 percent of a researcher's time. The salary for lower percent efforts would be prorated accordingly.

Dr. Michael John Becich, Chairman and Distinguished University Professor, Department of Biomedical Informatics, Professor, Pathology, Information Sciences, Telecommunications and Clinical/Translational Sciences, Associate Vice Chancellor for Informatics in the Health Sciences, Director, Center for Commercial Application of Healthcare Data, Associate Director for Cancer Institute (UPCI), Associate Director, Clinical and Translational Science Institute, University of Pittsburgh School of Medicine, suggested including additional data sets, such as clinical phenotyping, in the NCI informatics and big-data initiatives, as well as considering providing computational/informatics training within the new Cancer Center Support Grant training efforts for NCI-designated Cancer Center researchers and oncologists.

Dr. Ethan M. Basch, Professor of Medicine, Division of Oncology, School of Medicine, Professor of Public Health, Department of Health Policy and Management, Gillings Global School of Public Health, Director, Cancer Outcomes Research Program, Co-leader, Cancer Prevention and Controls Program, Lineberger Comprehensive Cancer Center, The University of North Carolina at Chapel Hill, asked about plans to integrate population science and big data. Dr. Sharpless offered two options the NCI might consider: (1) developing a large aggregated publicly available universal data set—cost, data types, privacy, and quality not withstanding; or (2) soliciting ideas from the health and population science communities via crowd funding on ways to approach this type of initiative.

Dr. David A. Tuveson, Roy J. Zuckerberg Professor, Director, Cold Spring Harbor Laboratory, encouraged the NCI to leverage the existing efforts of foundations (e.g., Stand Up to Cancer and the Parker Foundation) working with patient groups to share information on clinical best practices, such as new information on immunotherapies.

Dr. Timothy Ley, Professor of Medicine and Genetics, Division of Oncology, Department of Medicine, Washington University School of Medicine at St. Louis, lauded the NCI for increasing funding for K08 and K23 awards and noted the need for the NIH Center for Scientific Review (CSR) Study Sections to understand the new applications now that the two awards have been combined. Dr. Lowy explained that the CSR has been briefed on the changes to NCI's K08 and K23 awards.

IV. LEGISLATIVE REPORT—M. K. HOLOHAN

Ms. M. K. Holohan, Director, Office of Government and Congressional Relations (OGCR), reported on the budget, appropriations, and other legislation of interest. The current government funding will end in 9 days when the December 8, 2017 Continuing Resolution (CR) expires. The FY 2018 budget

approval may take longer than anticipated, and a CR extension is likely. If that happens, the NCI will remain at its FY 2017 spending level.

Ms. Holohan remarked on the strong congressional bipartisan support for the NIH and NCI and the many interactions between congressional staff and the NIH. In 2017, more than 20 members of Congress and 50 of their staff visited the NCI, including interest from such first-time visitors as the House Budget Committee staff.

Ms. Holohan informed members that Dr. Sharpless spoke on cancer immunotherapy and the related advances in NIH-funded research at the November 14, 2017, Senate NIH Caucus briefing hosted by co-chairs Illinois Senator Dick Durban and South Carolina Senator Lindsay Graham. He was joined by Dr. Rosenberg, CCR, and a former immunotherapy patient, Ms. Lindsay Condrey, who shared her story. Also, three extramural researchers—Dr. Thomas F. Gajewski, The University of Chicago, and Drs. Raymond N. Dubois and Chrystal Paulos, Medical University of South Carolina—shared their research experiences.

Ms. Holohan reminded members that the President's FY 2018 budget request released on May 23, 2017, includes a 20 percent decrease for the NIH budget compared to FY 2017. In July 2017, the House Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies advanced its bill out of committee to increase funding to the NIH by \$1.1 billion (B) and to the NCI by \$82 million (M). The Senate Appropriations Subcommittee advanced its bill out of committee in September 2017 to increase funding to the NIH by \$2B and to the NCI by \$169M. The House and Senate FY 2018 allowances, if approved, would mark the third consecutive year of increases for the NIH and NCI and signify the direction that should continue. The next steps for Congress will be to decide on a CR to keep the government operating, agree on the FY 2018 budget, prepare a FY 2018 omnibus spending bill, and prepare for a February 2018 (or later) release of the President's FY 2019 budget request. The appropriators are continuing to work, and the NIH and NCI remains hopeful for a timely decision.

V. PRESIDENT'S CANCER PANEL REPORT—DR. BARBARA K. RIMER

Dr. Barbara K. Rimer, Dean, Gillings School of Public Health, Alumni Distinguished Professor of Health Behavior and Health Education, The University of North Carolina at Chapel Hill, provided an update on the activities of the President's Cancer Panel (PCP, the Panel). She reminded members of the mission of the Panel, which is to monitor the development and execution of the activities of the National Cancer Programs and report directly to the President of the United States any barriers to the progress of those programs. In addition to Dr. Rimer, the Panel members include Mr. Hill Harper, cancer survivor, actor, and lawyer; and, until recently, Dr. Owen N. Witte, Clinical Scientist, University of California, Los Angeles, who resigned in August 2017. She expressed appreciation to Dr. Abby B. Sandler, Executive Secretary, PCP; PCP/NCI staff; and PCP contract staff for their support.

Dr. Rimer reported on the continued impact of the Panel's 2012–2013 Report to the President, "Accelerating Human Papillomavirus (HPV) Vaccine Uptake: Urgency for Action to Prevent Cancer." She discussed changes in the HPV vaccination landscape since the report was released and mentioned activities related to the Panel's report recommendations. In 2015, the Centers for Disease Control and Prevention (CDC) reported that the national HPV vaccination rate for adolescents between the ages of 13 and 17 was 56 percent for males and 65 percent for females. In December 2016, CDC's Advisory Committee on Immunization Practices recommended a two-dose schedule with the 9-valent HPV vaccine. The NCI, in collaboration with the Bill and Melinda Gates Foundation (Gates Foundation), is conducting a randomized control trial (RCT) to evaluate a one-dose regimen of HPV vaccine for durable protection against cervical cancer.

Dr. Rimer presented the recommendations of the Panel’s 2016 Report to the President, “Improving Cancer-Related Outcomes with Connected Health.” Workshop series co-chairs, Drs. David K. Ahern, Director, Program in Behavioral Informatics and eHealth, Brigham and Women’s Hospital, and Bradford W. Hesse, Division of Cancer Control and Population Sciences (DCCPS), NCI, led this effort. The report recommendations focus on five priority areas: interoperability; individuals, patients, and caregivers; cancer workforce; Internet access; and data sharing and integration, which were formalized into individual objectives with associated action items.

Dr. Rimer was joined by Dr. Hesse, who described the newly established public-private partnership between the Federal Communications Commission (FCC) and the NCI. Dr. Hesse noted that the NCI worked with the FCC Task Force, Connect2Health, which was established by then-FCC chairman, Tom Wheeler, to accelerate the adoption of health care technologies by leveraging broadband and other next-generation communication services. The current FCC chairman, Ajit Pai, has endorsed the Taskforce and NCI’s efforts that are included in the 2016 Report to the President on connected health. Catalyzed by the Cancer MoonshotSM activities, the PCP and NCI recognized the need to foster collaborations across different organizations to achieve these goals. A memorandum of understanding (MOU) between the NCI and the FCC was drafted with the intent to share data on the convergence of broadband regarding cancer mortality, late-stage occurrences, and treatment using Surveillance, Epidemiology and End Results (SEER) registry data; conduct pilot and demonstrations projects in rural areas, beginning in the Appalachian region and the state of Kentucky; and jointly hold meetings within national areas.

Dr. Rimer reminded members that the 2016–2017 workshop series, “Ensuring Patients Access to High-Value Cancer Drugs,” included three workshops led by series co-chair, Dr. Gary Gilliland, President and Director, Fred Hutchinson Cancer Research Institute; and DCCPS Liaison, Dr. Ann Geiger, Deputy Associate Director, Healthcare Delivery Research Program (HDRP). The second workshop in the series, “Emerging Opportunities to Streamline Cancer Drug Development,” was held on December 9, 2016, and participants discussed the disease treatment potential of precision cancer medicine; policies and strategies to ensure patient access to new therapies; and key actions that could streamline the drug development and approval processes. The third and final workshop in this series, “Pricing and Payment Strategies for Cancer Drugs: Maximizing Patients’ Access to Beneficial Therapies,” was held on March 27, 2017. The workshop focused on understanding value-based pricing in cancer treatment and response to treatment, strategies to reduce financial toxicity to patients, and factors influencing drug pricing and payment. The content for the report on this Panel series, the 2018 Report to the President, “Navigating the Era of High-Cost Cancer Drugs: An Urgent Call to Promote Value, Ensure Access, and Minimize Financial Toxicity,” is expected to be released in February 2018. Dr. Rimer called attention to a soon-to-be-released report by the National Academies of Sciences, Engineering, and Medicine— “Making Medicines Affordable: A National Imperative”—which aligns with the activities of the Panel.

Questions and Answers

Dr. Electra D. Paskett, Marion N. Rowley Professor of Cancer Research, Director, Division of Cancer Prevention and Control, Department of Internal Medicine, College of Medicine, The Ohio State University, noted that the national HPV adolescent vaccination rates quoted were the rates for those receiving one of the three doses of the HPV vaccine. The reported rates of those receiving all the recommended HPV doses are lower, at 28 percent for males and 42 percent for females.

Dr. Karen M. Emmons, Dean for Academic Affairs, Office of the Dean, Harvard T. H. Chan School of Public Health, asked about the effect of the potential rollback of the FCC net neutrality legislation on the connected health initiatives. Dr. Rimer speculated that there would be an impact, but the NCI has not had those discussions.

In response to a query by Dr. Seewaldt on whether the Panel would address the potential use of low-cost repurposed drugs for early detection (i.e., precision prevention), Dr. Rimer agreed that precision prevention would be a topic to consider for the future, but it is outside of the scope of the 2018 report.

Dr. Basch asked about actions that could be rapidly implemented regarding connected health, interoperability, and barriers that align with the Cancer MoonshotSM initiatives and NCI's new big-data and data integration goals. Dr. Rimer explained that the PCP was represented on the BRP and worked to ensure that the MoonshotSM recommendations were consistent with the Panel's reports. Dr. Hesse added that the 21st Century Cures Act passed in December 2016 contains stipulations against data blocking and encourages the use of health information technology. Also, the NCI is exploring existing electronic health records platforms and standards, including Substitutable Medical Apps and Reusable Technology (SMART) and Fast Healthcare Interoperability Resources (FHIR[®]).

VI. RECOGNITION OF RETIRING BSA MEMBERS—DR. NORMAN E. SHARPLESS

On behalf of the NCI, Dr. Sharpless recognized the contributions made by members of the BSA whose terms of office have expired. He expressed appreciation for their service and dedication over the course of their terms. The following BSA members are retiring: Drs. Sangetta N. Bhatia, John J. and Dorothy Wilson Professor, Division of Health Sciences and Technology and Electrical Engineering and Computer Science, Institute for Medical Engineering and Science, Koch Institute for Integrative Cancer Research, Broad Institute, Brigham and Women's Hospital, Massachusetts Institute of Technology; Daniel C. DiMaio, Waldemar Von Zedtwitz Professor and Vice Chairman of Genetics, Department of Genetics, Professor of Therapeutic Radiology and Molecular Biophysics and Biochemistry, Deputy Director, Yale Cancer Center, Yale University School of Medicine; and Chanita A. Hughes-Halbert, Professor and Endowed Chair, Department of Psychiatry and Behavioral Sciences, Hollings Cancer Center, Medical University of South Carolina,.

VII. HIGH-QUALITY RISK-BASED CERVICAL CANCER SCREENING FOR THE UNITED STATES AND THE WORLD—DRS. MARK C. SCHIFFMAN AND NICOLAS WENTZENSEN

Dr. Mark C. Schiffman, Senior Investigator, Clinical Genetics Branch (CGB), Division of Cancer Epidemiology and Genetics (DCEG), NCI, presented on high-quality risk-based cervical cancer screening for the United States and the world. Dr. Lowy prefaced the presentation by remarking that although the industrialized world has made great strides in the past 60 years in focusing on high-quality screening for cervical cancer (e.g., Papanicolaou test [Pap test]), the opportunities for such in the developing world are lagging. The NCI is optimistic that through support of research for technology development and increased understanding of the biology and the etiology of cervical cancer, successful strategies will lead to enabling high-quality cervical cancer screening in most countries in the world.

Dr. Schiffman remarked that preventing cervical cancer has been successful in many high-resource countries, and new strategies can significantly increase this reach of prevention, yet the burden worldwide is still increasing. More than 12 types of HPV have been shown to cause cancer, and progression varies by type. Persistent HPV type 16 (HPV 16) is the major determinant linked to cervical cancer. Persistent HPV infection (i.e., 7 years post infection) leads to the pre-cancerous state, and further genetic alterations are necessary for invasive cancer. This long latency period provides opportunities for screening and treatment. Most of the HPV-related cervical cancers are reported in low- and middle-income countries (LMIC) and account for 90 percent of cancer deaths.

Dr. Schiffman reminded members that NCI's cervical cancer prevention research began in 1980 with a discovery phase and mechanistic studies; the prevention methods phase, including HPV test

validations and pivotal HPV vaccination clinical trials, spanned from 1995 to 2005. After successfully achieving a promising vaccine against HPV, the challenge was to implement a three-dose regimen and screening methods in low-resource countries. A resurgence in 2010 to the present brought about the practical strategies phase, in which the knowledge of HPV and cervical carcinogenesis began to affect the reduction in cervical cancer to the extent of producing guidelines and one-dose vaccines.

Dr. Schiffman explained that the highly complex organizational and societal cervical cancer screening needs to be simplified and/or deconstructed. Traditional clinically used classifications, such as the Bethesda System, may need to be revisited or updated based on new insights into the molecular mechanisms. A simplified screening model would need to involve assessing normal cervix, high-risk HPV-infected cervix, precancerous cervix, and cancerous cervix—using cytologic, molecular, and/or visible methods. Preventing cervical cancer involves interventions at each step of HPV natural history. For example, a vaccine administered during the peak prevalence period and screening to detect precancerous lesions would essentially eliminate cancer. He touched briefly on a scientific evaluation of one or two doses of the HPV vaccines, a current collaboration between NCI investigators (Drs. Aimee R. Kreimer and Allan Hildesheim, DCEG), Costa Rican investigators, and the Gates Foundation.

Dr. Schiffman introduced the proposed cervical cancer screening approach—precision prevention—the goal of which is to detect and treat true precancer while minimizing over-treatment. The challenge, primarily in low-resource countries, has been to determine the next steps (treatment strategy) when a person has tested positive for HPV, which would be to determine the intervention based on the HPV natural history and apply the appropriate treatment strategy. Evidence from supporting studies conducted by DCEG investigators has shown that the HPV test alone is more sensitive than the Pap test (i.e., cytology), which also did not offer an advantage in cotesting (HPV plus cytology).

Dr. Nicolas Wentzensen, Deputy Branch Chief, Senior Investigator, CGB, DCEG, discussed the cervical cancer screening program. Three strategies are approved in the United States, a high-resource setting: cytology, HPV testing, and cotesting. Each can identify the subset of the population at increased risk for developing cancer, but many of the women testing positive will not progress to the precancerous stage. A two-step process—a triage test on the initial cervical sample, followed by a diagnostic colposcopic biopsy—is used to decide who among the screen-positives needs treatment. In low-resource settings, the HPV test and/or visual inspection with acetic acid (VIA or visual) have been the primary screening strategies that have been evaluated by NCI-sponsored demonstration projects. The low sensitivity, lack of specificity, and irreproducibility of the visual or molecular triage presents a challenge to the diagnosis and treatment of screen-positives. These types of evaluating projects and triage strategies are ongoing.

Dr. Wentzensen described the NCI's risk-based approach to screening and management of cervical cancer, which consists of four categories: minimal risk, screening in regular 3- to 5-year intervals is recommended; low risk, triage or repeat testing occurs; medium risk, a colposcopy is performed; and high risk, treatment is required. In low-resource settings, the infrastructure does not support medium-risk screenings. Only two approaches are available: no treatment in low-risk cases in which thresholds are being developed or treatment in high-risk cases. Triage strategies include cytology-based methods, which are used in high- and middle-resource settings; molecular tools that are applicable in all settings; and visual methods common to low-resource settings. Although cytology-based triage for identifying HPV-positive women is being considered as a secondary test in many international guidelines, the underlying problems of low sensitivity and non-specificity remain. To address these issues, the DCEG introduced a precision-prevention application, automated cytology, which uses machine-learning-based scoring for risk stratification in HPV-positive women. Furthermore, the NCI in collaboration with Kaiser Permanente Northern California (KPNC) and Heidelberg University evaluated molecular markers of HPV oncogenic activity—P16, an HPV E7 specific marker, and Ki 67, a cellular proliferation marker—in large cohort

studies. These are approaches can be implemented now.

Dr. Wentzensen pointed out that molecular triage tools, such as HPV genotyping and DNA methylation methods, which would be applicable in high- and low-resource settings, also are being developed. For example, leveraging the recent TCGA findings from the integrated genomic and molecular characterization of cervical cancers, the DCEG currently is focusing molecular marker discovery efforts within the Study to Understand Cervical Cancer Early Endpoints and Determinants (SUCCEED) on investigating the integrated characterization of cervical precancers. Also, an ongoing collaboration with Dr. Robert D. Burk at the Albert Einstein College of Medicine to develop assays to interrogate methylation in the HPV genome and its association to cervical precancer is expected to culminate in an integrated next-generation-based HPV detection, genotyping, and methylation assay that would allow additional risk stratification to be done on one specimen.

Members were informed that development of new technology, including automated image analysis to improve visual triage in low-resource settings, is in progress. To support this initiative, the NCI is providing a colposcopy database of more than 100,000 images for training and validations, and extramural partners in academia, nonprofit organizations, and industry are participating in a machine learning challenge. Evaluations are being conducted in specific countries including the United States, El Salvador, and countries in Africa. Efforts to improve visual triage in high-resource settings also are underway. The NCI Biopsy Study, which focused on evaluating the performance of the colposcopy in the United States, resolved many of the underlying issues. The NCI has since worked with scientific societies, including the American Society for Colposcopy and Cervical Pathology, to develop the first U.S. colposcopy guidelines, which were published in 2017. Lastly, large-scale evaluation of these screening triages and strategies in an Improved Risk-Informed HPV Screening (IRIS) study in collaboration with KPNC is in progress. The goals of this work are to inform screening and management guidelines for the United States and the world; integrate vaccination and screening; and adopt/develop a comprehensive program applicable to every setting, regardless of level of resources.

Questions and Answers

Members lauded the DCEG and the NCI for their ongoing efforts to improve cervical cancer screening and diagnosis worldwide.

Dr. Maria Elena Martinez, Professor, Department of Family Medicine and Public Health, Program Leader, Reducing Cancer Health Disparities, Sam M. Walton Endowed Chair for Cancer Research, Moores Cancer Center, University of California, San Diego, asked about strategies (e.g., self-sampling, vaccination, primary prevention) to address the needs of patient populations in low-income regions in the United States (e.g., along the U.S.-Mexico border) where access to cervical cancer screening is limited. Dr. Schiffman explained that the issues are regulatory—related to U.S. Food and Drug Administration (FDA) -approved technologies, custody, and counseling—not issues in specific U.S. populations' use of the technology. Implementation and regulation of the tools/technologies would need to be addressed.

In response to comments from Dr. Paskett on implementation plans that are affordable and include individual-based risk factors that are representative of the local populations in the screening algorithms, Dr. Schiffman pointed out that consensus guidelines are established involving representatives from 25 different clinical organizations, who provide input on acceptability and thresholds. Efforts are ongoing with technology developers to ensure that costs for the end-user remain low for any technologies or assays being developed. Dr. Wentzensen added that assessment of other risk factors in the large cohort studies with KPNC were not as prominent as the molecular markers. Dr. Schiffman called attention to a long-term HPV cofactor project, which will provide insight into other risk factors meriting consideration.

Dr. DiMaio asked about the length of time from development of the HPV methylation assay to its availability in a low-resource setting. Dr. Wentzensen responded that assay development is in still progress and that the NCI is working with Global Good, a company specializing in inventing technologies for low-resource settings, to adapt the HPV methylation assay post development.

Dr. Karlan commented that conducting smaller implementation projects, working with professional organizations, engaging patients and patient advocacy groups, and providing educational tools would be ways to ensure that the implementation plan for the new screening guidelines in low-resource settings is cost efficient and not a burden to the existing infrastructure. Dr. Schiffman noted that the DCEG is working with the Cancer Intervention and Surveillance Modeling Network (CISNET) regarding cost-effectiveness.

Dr. Ian M. Thompson, Jr., President, CHRISTUS Santa Rosa Medical Center Hospital, Texas Urology Group, asked how the local culture and policy might affect implementing an HPV vaccination program. Dr. Schiffman replied that the objective is to integrate cervical cancer screening and HPV vaccination into one program. Also, emphasizing the outcome, a devastating disease, cervical cancer, and deemphasizing the sexually transmitted disease, HPV, is another strategy.

Dr. Francis Ali-Osman, Margaret Harris and David Silverman Distinguished Professor of Neuro-Oncology, Professor of Surgery, Professor of Pathology, Department of Surgery and Pathology, Duke University Medical Center, asked about the mechanisms associated with the HPV screen-positive cases that do not progress to cancer. Dr. Wentzensen explained that only 30 percent of cervical precancers will progress to cancer. Evidence suggest that genotypes, host factors, or cell-mediated immunity may play a role. Ideally, the DCEG would want to focus on those precancerous cases that are likely to progress to cancer, with the anticipation that ongoing studies of the viral and host genomes would provide new insights into the disease progression.

Dr. Robert Croyle, Director, DCCPS, commented on the feedback from the immunization and primary care communities and local state health departments on the impact of visible leadership from the cancer community, including NCI-designated Cancer Center directors and clinicians, to the success of a pediatric vaccination program. This visible presence and engagement, partly due NCI's investments, will be the level necessary to promote the implementation phase as well.

VIII. PATIENT-REPORTED OUTCOMES VERSION OF THE COMMON TERMINOLOGY CRITERIA FOR ADVERSE EVENTS (PRO-CTCAE™)—DRS. PAUL JACOBSEN, SANDRA A. MITCHELL, AND LORI MINASIAN

Dr. Paul Jacobsen, Associate Director, Healthcare Delivery Research Program (HDRP), DCCPS, provided an overview of the NCI PRO-CTCAE™, a measurement tool. As a standard set of criteria used to classify adverse events of drugs used in cancer therapy, Common Terminology Criteria for Adverse Events (CTCAE) is based on laboratory findings, clinical observations, and other data sources. Clinical investigators or the research staff assess the severity of each adverse event (AE) using a 5-point grading scale. The challenge to using CTCAE alone is that approximately 10 percent of the 800 AEs listed are symptoms (e.g., pain, fatigue, or nausea), and patient self-reporting (i.e., patient-reported outcomes [PROs]), not clinician grading, is considered the gold standard for assessing these symptoms. The PRO-CTCAE™, which was designed as a companion to the CTCAE, consists of 78 symptomatic AEs drawn from the CTCAE that were used to develop an item library of questions for building customized patient surveys that can be administered either on paper or electronically.

Dr. Jacobsen reminded members that the NCI awarded two contracts for the development and testing of PRO-CTCAE™; the first award was made in 2008 and the second in 2010. He acknowledged Dr. Basch, who played a key role in the validation of the PRO-CTCAE™ item library and feasibility testing in cooperative group trials. In 2011, the initial library was made available, and early adopters in 12 countries joined in operational testing of the PRO-CTCAE™ in clinical trials. The PRO-CTCAE™ was made publicly available in April 2016. To date, it has been incorporated into 20 NCI-sponsored trials and more than 125 industry-sponsored studies, is employed in several population-based registry studies, and has been translated into multiple languages. Many agencies, divisions, organizations, and partners have supported the development and use of PRO-CTCAE™, including NCI's DCCPS, Division of Cancer Prevention (DCP), DCTD, and CBIIT; FDA's Oncology Center of Excellence (OCE) and Center for Drug Evaluation and Research; together with academic, advocacy, industry, and international partners.

Ongoing Development of PRO-CTCAE: Broadening Applicability and Interpretability in Cancer Clinical Trials. Dr. Sandra Mitchell, Program Director, HDRP, DCCPS, elaborated on the ongoing development of PRO-CTCAE™ and its broadening applicability and interpretability in cancer clinical trials. Measuring safety and tolerability in cancer clinical trials is fundamental to drawing conclusions about the effectiveness of cancer therapies. Real-time ascertainment using PROs can improve the precision and reproducibility of symptomatic AE reporting, which is what the PRO-CTCAE™ hopes to achieve. Version 1 of the PRO-CTCAE™ Measurement System consists of an item library of 78 PRO-CTCAE™ symptom terms. Investigators build study-specific custom surveys by selecting the symptom terms that reflect the anticipated toxicities of the therapy being studied. Conditional branching (i.e., patterns to skip) within PRO-CTCAE™ surveys helps to limit patient burden.

Dr. Mitchell detailed several design principles with respect to inclusion of PRO-CTCAE™ in cancer clinical trials. PRO-CTCAE™ is designed to be used in conjunction with CTCAE; the timing of assessments should be comparable and data reporting should be done in parallel. Properly conducted item selection and assessment timing reduces bias and maximizes the interpretability and utility of the results. She noted that PRO-CTCAE™ items distinguish the attributes of frequency, severity, and/or interference separately for each toxicity; CTCAE collectively evaluates these attributes using standardized criteria and assigns a single grade (grade 0–5) that reflects both increasing severity and clinical actionability. She underscored the fact that a PRO-CTCAE™ score is not equal to a CTCAE grade. Up to three patient-reported scores per symptomatic toxicity are recorded. The HDRP currently is investigating ways to combine the different attributes and strategies for interpretation of those scores.

Dr. Mitchell informed members that the PRO-CTCAE™ public website averages 671 visits each month. Since the initial release, additional resources have been added and the Instrument and Form Builder components are available in seven validated languages. To date, more than 200 studies are registered in PRO-CTCAE™, representing more than 60 institutions, organizations, and research sites. A January 2018 update will include the release of an additional eight linguistically validated languages. Another six languages are currently undergoing linguistic validation and are anticipated for release by August 2018. She reported that the interpretation and clinical utility of PRO-CTCAE™ is still evolving. Efforts to enhance access, interpretability, and utility are ongoing. Activities include testing PRO-CTCAE™ responsiveness to change, engaging adopters in a variety of oncology subspecialties to expand the item library, working on technologies to optimize acceptability in clinical workflow, and psychometric testing of a pediatric version of PRO-CTCAE™. Dr. Mitchell remarked that a Cancer MoonshotSM FOA to strengthen the analysis and interpretation of CTCAE and PRO-CTCAE™ has been issued.

Inclusion of PRO-CTCAE™ in NCI-Sponsored Clinical Trials and Regulatory Considerations. Dr. Lori Minasian, Deputy Director, DCP, reported that of the 20 trials within the NCI NCTN that have incorporated PRO-CTCAE™, 10 are Phase III studies, eight are Phase II studies, one is

a Phase II/III study, and one is a Phase I study. To date, 13 trials are active; four are ongoing, but are closed to accrual; one is closed to accrual and treatment, but study responses have not been reported; one is completed, except for the FDA requirements; and one is fully complete. The most commonly measured symptomatic AEs include diarrhea, nausea, fatigue, and pain; these could be the result of the tumor itself or the treatment under investigation.

Dr. Minasian informed members that a prototype system was developed to capture PRO-CTCAE™ data electronically and was initially tested in two large multisite NCI-sponsored feasibility studies and several other smaller studies proposed by early adopters. Four studies are continuing to use the prototype. While useful for these feasibility studies, the prototype is not scalable, and data analysis and interpretation were limited by the fact that the prototype application houses the PRO-CTCAE™ data separately from the other trial data. The NCI-sponsored clinical trials networks use Medidata Rave® as the remote data capture system, and thus DCP and CTEP have implemented the electronic PRO (ePRO) module for Rave. Since August 2017, a Rave library of PRO-CTCAE™ items in English and Spanish has been available for the NCI clinical trials groups to create trial-specific PRO-CTCAE™ surveys for use through ePRO.

Dr. Minasian informed board members that NCI staff have been working with the FDA to address data standards, interpretability, and regulatory concerns with respect to the inclusion of PRO-CTCAE™ in cancer clinical trials. In parallel, collaborations with the FDA and patient advocacy groups, including the Critical Path Institute and Friends of Cancer Research, have helped to highlight PRO-CTCAE at annual meetings and workshops and facilitate the activities of the PRO-CTCAE™ Industry Working Group. To address the regulatory issues regarding safety reporting, the FDA, NCI, and the Office of Human Research Protection, Department of Health and Human Services, met in April 2017 to focus on the implications of PRO-CTCAE™ for clinical review, investigational new drug safety reporting, and clinical site inspections. The meeting outcomes are soon to be published.¹ The next steps will be to develop methods for analysis of CTCAE and PRO-CTCAE™ data; the Cancer MoonshotSM RFA-CA-17-052 will be one such mechanism to begin this type of analysis.

Dr. Minasian then called upon Dr. Paul Kluetz, Associate Director, OCE, FDA, who briefly discussed PRO-CTCAE™ in cancer clinical trials. He remarked that the greatest challenge the OCE has observed with PRO-CTCAE™ and cancer clinical trials is the use of a generic off-the-shelf tool to explain the symptoms from two types of drugs. The OCE underscored the value and flexibility of the PRO-CTCAE™ Measurement System's item library model in that it allows each study to monitor the toxicities relevant to the therapy under study, while at the same time limiting patient burden. Commercial sponsors of clinical trials share the same regulatory concerns as previously discussed regarding safety reporting and site inspections, and Dr. Kluetz commented that NCI and FDA have been working closely with representatives from academic settings, the cooperative groups, and industry sponsors to achieve consensus around best practices and study design principles when PROs are included to capture symptomatic toxicities.

¹ The meeting report was published December 13, 2017.

Kim, J., H. Singh, K. Ayalew, et al. 2017. "Use of PRO Measures to Inform Tolerability in Oncology Trials: Implications for Clinical Review, IND Safety Reporting and Clinical Site Inspections." *Clin Cancer Res* December 13 2017 doi: 10.1158/1078-0432.CCR-17-2555.

Questions and Answers

Dr. Mack Roach III, Professor of Radiation Oncology and Urology, Director, Particle Therapy Research Program and Outreach, Department of Radiation Oncology, University of California, San Francisco, Helen Diller Family Comprehensive Cancer Center, asked about the inclusion of radiation-induced toxicities in the PRO-CTCAE™. Dr. Minasian explained that some items included in the PRO-CTCAE™ item library reflect the anticipated toxicities of radiation therapy and noted that one of the early studies testing the feasibility of PRO-CTCAE™ was a radiation treatment trial. Dr. Mitchell called attention to a soon-to-be-published study that demonstrates that PRO-CTCAE™ has strong content validity as a measure of symptomatic toxicities in patients receiving radiation therapy and provides empirical support for the definition of site-specific PRO-CTCAE™ item sets to assess the symptomatic toxicities of radiation therapy.

Dr. Deborah Watkins Bruner, Robert W. Woodruff Chair of Nursing, Nell Hodgson Woodruff School of Nursing, Associate Director for Outcomes Research, Winship Cancer Institute, Emory University, encouraged the NCI to revisit the work published in 2014 to define core symptoms for inclusion in NCI clinical trials that include a PRO. Dr. Minasian agreed that this could be informative with respect to PRO-CTCAE item selection. Dr. Mitchell added that references to this work would be included in the resources available at the PRO-CTCAE™ website, thereby calling attention to this prior work to define a core set of symptoms that cross-cut cancer sites and treatment approaches.

In response to a query from Ms. Smith on encouraging researchers who are apprehensive about using PRO-CTCAE™ in clinical practice, Dr. Minasian replied that the interest in using the PRO-CTCAE™ is high and noted that the frequent visits to the public website are evidence that adoption of PRO-CTCAE™ across a variety of cancer treatment settings is expanding steadily. Helping physician-investigators and others understand how they would use the information could further accelerate its uptake. The Cancer MoonshotSM RFA is expected to increase response to the use of PRO-CTCAE™ data in trials. Dr. Jacobsen added that a second MoonshotSM RFA has been issued to address the inclusion of systematic symptom surveillance (including the use of PRO-CTCAE™) and guideline-concordant symptom management into clinical practice routines.

Dr. Basch encouraged the NCI to revise the language of the PRO-CTCAE™ license so that it allows real-world use of the tool in clinical practice without any restrictions on the website license and to consider removing this language from the NCI website. Dr. Basch also noted that the translations have been funded by pharmaceutical companies, rather than by the NCI. Industry-sponsored clinical trials that are conducted internationally would require additional translations of the PRO-CTCAE™. He encouraged the NCI to consider increasing funding to support such translations. In addition, Dr. Basch suggested that the NCI provide funding support to the NCTN research bases to support the administrative personnel necessary for the implementation and administration of this tool in NCTN trials, move oversight of the CTCAE and PRO-CTCAE™ to the CTEP, and continue DCP oversight of future research on the PRO-CTCAE™. Without these changes, there is a risk that this tool, which the NCI has invested in over the past decade and which can increase the patient-centeredness of drug development, might not be successfully disseminated.

IX. EARLY CAREER INVESTIGATORS AND NCI PLANNING—DR. L. MICHELLE BENNETT

Dr. L. Michelle Bennett, Director, Center for Research Strategy (CRS), NCI, presented NCI's planning process and proposal for ECIs. In the spring of 2017, the NIH proposed using the GSI, a process to fund additional ESIs by limiting the total number of grants to any one individual. Following a period of discussions with the cancer community, the NIH proposed the Next-Generation Researchers Initiative

(NGRI) in June 2017. The NIH released the NGRI policy on August 31, 2017, which implements, in part, *Section 2021* of the 21st Century Cures Act. The NIH NGRI policy implements prioritizing funding for ESI applications with meritorious scores. ESIs are investigators who have completed a terminal degree or clinical training within the past 10 years and have not successfully competed for substantial NIH funding. The policy also establishes and prioritizes funding for a new category of investigator, Early Established Investigators (EIs), who have received a first substantial NIH competing award within the past 10 years. The NIH's stated goals for FY 2017 are to fund 200 additional ESIs and 200 additional EIs above the FY 2016 funding levels. NIH's Institutes and Centers (ICs) were given funding targets, and the NCI awarded 10 percent more ESI applications in FY 2017 than in FY 2016.

Dr. Bennett reported on NCI's implementation of the NGRI. The CRS began an in-depth review of the NCI-funded workforce, with special emphasis on the ESIs, and used a data-driven approach in its decision-making process for planning changes to the support of early career investigators. An internal NCI ESI Working Group, composed of NCI leadership, was convened in September 2017 to review the data, develop policies, and develop an approach to support early career investigators. The outcome was a proposed pilot approach for the NCI to continue to fund additional Research Project Grant (R01) applications for early career investigators and adopt a six-point plan for extending special consideration to early career investigators. R01 applications receiving a meritorious score and having no major flaws for exceptions will be considered.

Dr. Bennett outlined the NCI's six-point pilot proposal for early career investigators and provided supporting data.

1. **Establish the NCI Early Career Investigator (ECI).** An ECI is defined as a principal investigator who is 15 years past his or her terminal degree or clinical training. The CRS data analysis revealed that the median time from degree to a first NCI R01 award has progressively increased over time from 6 years in 1980 to more than 10 years in 2016. This trend suggests that a 15-year cut-off stipulation would be reasonable, which the NCI is proposing. This approach more directly benefits Ph.D. investigators.
2. **Award successful ECI applications for 5 plus 2 years.** The NCI proposes funding ECIs for 5 years, plus an additional 2 years. CRS's data analysis of three NCI R01 awardee cohorts—FY 1997, FY 2007, and FY 2011—shows that 40 percent of FY 1997 awardees, 25 percent of FY 2007 awardees, and 29 percent of FY 2011 awardees continued to receive NCI R01 funding 5 years after their first awards. Furthermore, of the funded FY 2011 NCI R01 awardees, 14 percent had not submitted an R01 application and 45 percent had, but were not successful. The NCI hopes that this 5- plus 2-year approach will shift these trends.
3. **Provide mentoring for ECIs.** Expand support for ECIs who receive 5- plus 2-year awards with intensive mentoring and training from the NIH and engagement from their institutions. The NCI will need to develop strategies to evaluate the effectiveness of the mentoring and training approaches.
4. **Continue to expand efforts to increase diversity of the NCI-funded workforce.** The CRS's review showed that for ESIs and established investigators, the funding rate of underrepresented groups (URGs) is significantly lower than that of whites, the overall percentage of NCI R01 principal investigators from URGs is very low, and representation of women in the overall NCI R01 pool is significantly lower than that of men. The NCI is open to suggestions for additional approaches to increase diversity of the NCI-funded workforce. An ECI-specific program notice that would model the successful NCI Diversity Supplements is one example.

5. **Continue to emphasize bridge awards (R56) and funding by exception for any principal investigator at risk of losing all substantial funding.** Any established investigator with a meritorious R01 application who is at risk of losing all substantial funding will be considered, regardless of career stage. Other NIH ICs are using this approach in implementing the NGRI.
6. **Fund more R01 applications from ECIs.** The NCI will focus on funding more applications as the budget allows. The applications should have received a meritorious score (e.g., 25th percentile or higher) and have no major flaws to be considered for exception pay.

Dr. Bennett remarked that the NCI will continue to monitor and evaluate over time the impact of these approaches. She expressed appreciation to the CRS data analysis team and the NCI ESI Working Group for supporting this effort.

Questions and Answers

In response to a query from Dr. Seewaldt, Dr. Bennett replied that the pilot proposal does not include funds for mentors, but compensating established investigators for mentoring is something that the NCI could discuss.

Dr. Ley encouraged the NCI to consider extending the terms for mentored and individual research support for the Pathway to Independence Awards (K99/R00) in the pilot proposal, which would align with the 2014 Physician-Scientist Working Group recommendations. He also suggested leveraging the award programs tracking system being developed by the Office of Extramural Programs.

Dr. Cheryl L. Walker, Director, Center for Precision Environmental Health, Professor, Department of Molecular and Cellular Biology, Baylor College of Medicine, asked about the feasibility of using these data on the ESIs to predict an investigator's success of a second NCI R01. Dr. Bennett explained that a review of the productivity trends of NCI-funded investigators using bibliometrics did not show a correlation. These data analysis are still new, and the next steps will need to be considered.

Dr. Peter C. Adamson, Chair, Children's Oncology Group, Alan R. Cohen Endowed Chair in Pediatrics, The Children's Hospital of Philadelphia, University of Pennsylvania, commented that without addressing the cause of the delay to a first R01, extending the cut-off period to 15 years may further compound the problem.

Dr. Robert D. Schreiber, Andrew M. and Jane M. Bursky Distinguished Professor, Department of Pathology and Immunology, Director, The Andrew M. and Jane M. Bursky Center for Human Immunology and Immunotherapy Programs, Program Co-leader, Tumor Immunology, Washington University School of Medicine, encouraged the NCI to investigate alternative explanations for the increase in time from terminal degree to a first NCI R01 award for ESIs. Other factors, such as the NCI budget and the ease of securing a new grant versus a recompetition, should be considered. Establishing a working group to address this issue could be helpful.

X. RFA/COOPERATIVE AGREEMENT (COOP. AGR.) CONCEPTS—NEW AND RE-ISSUE—NCI STAFF

Office of the Director

**Investigation of the Transmission of Kaposi Sarcoma-Associated Herpesvirus (KSHV) (New RFA)
—Dr. Rebecca Liddell Huppi**

Dr. Rebecca Liddell Huppi, Program Director, Office HIV and AIDS Malignancy (OHAM), presented a concept to investigate the transmission of KSHV. The concept was proposed in collaboration with OHAM, DCP, DCCPS, the Division of Cancer Biology (DCB), and the National Institute of Dental and Craniofacial Research (NIDCR). The purpose of the RFA is to enhance understanding of the modes of KSHV transmission, with the overall goal of preventing KSHV infections, Kaposi sarcoma (KS), and other KSHV-induced diseases in populations living with HIV or at high risk for developing HIV. Dr. Huppi stated that KSHV is the causative agent of KS, which is one of the most common HIV malignancies worldwide and the most prevalent HIV-associated malignancy in sub-Saharan Africa. Approximately 44,000 new cases are reported annually, and more than 90 percent occur in low- to middle-income countries.

Dr. Huppi informed members that the predominant modes of KSHV transmission, the biology of the initial steps of infection, and risk factors for infection are not well understood. In endemic areas, such as sub-Saharan Africa, acquisition is believed to spread primarily by saliva exchange. In non-endemic areas, sexual transmission appears to be the primary route of transmission. KSHV could be prevented by decreasing the potential for an infection, developing a KSHV vaccine, or reducing the spread of KSHV through public health measures aimed at blocking the most important routes of transmission. This RFA concept aligns with the 2013 and 2017 recommendations of the BSA *ad hoc* Subcommittee on HIV and AIDS Malignancy.

The RFA would support research to improve understanding and advance knowledge of KSHV transmission to inform strategies to prevent KSHV transmission. The NCI-appropriated AIDS funds, as established by the NIH Office of AIDS Research (OAR), will support this research.

Subcommittee Review. Dr. Seewaldt expressed the Subcommittee's support for this concept, which addresses the important topic of KSHV transmission, particularly regarding viral latency and the increasingly aging HIV population. Dr. Seewaldt stated that the Subcommittee appreciates NCI staff responses to their requests to increase the focus of the RFA and to clarify the deliverables. She noted that special allocation of funds is appropriate, and addressing an issue identified by an independent body of experts is very responsive.

The first-year cost for the one-time issuance is estimated at \$4.5M for 8 to 10 awards, with a total cost of \$22.5M for 5 years.

Questions and Answers

Dr. Schreiber commented that given the nature of this research to focus on the basic virology and immunology of KSHV and not cancer, it would seem logical for these efforts to be investigated by the National Institute of Allergy and Infectious Diseases (NIAID) or private organizations that already are invested in research on the gamma herpes viruses, such as the Gates Foundation. He encouraged the NCI to focus the RFA on the cancer, not the KSHV infection. Dr. Robert Yarchoan, Director, OHAM, informed members that the KSHV-induced diseases are cancers and those cancers, including KS, have historically been studied within the NCI, which has the expertise and benefits from studying the virus and

the cancer. Dr. Lowy added that although the focus is on virology, this RFA is within the scope of what the NCI does for KSHV research.

In response to a query by Dr. DiMaio, Dr. Yarchoan explained that studies investigating KSHV transmission are complex and challenging. Because these studies involve human subjects and epidemiology, traditional virology laboratories working on KSHV are less likely to focus on studies to better understand the modes of transmission.

Motion. A motion to concur on the Office of the Director's (OD) Request for Application (RFA) entitled "Investigation of the Transmission of Kaposi Sarcoma-Associated Herpesvirus (KSHV)" was approved unanimously.

**Small Business Innovation Research (SBIR) Phase IIB Bridge Awards to Accelerate the Development of Cancer-Focused Technologies Toward Commercialization (Re-Issue RFA)
—Dr. Todd Haim**

Dr. Todd Haim, Program Director, Small Business Research Development Center, OD, NCI, presented a reissue concept for the SBIR Phase IIB Bridge Awards to accelerate the development of cancer-focused technologies toward commercialization. Dr. Haim stated that the SBIR and Small Business Technology Transfer (STTR) are two congressionally mandated programs in which federal agencies must devote a percentage of their extramural research budget to funding small businesses that meet their agency's mission. Congress structured the SBIR program into phases: Phase I, a proof-of-concept study, provides up to \$300,000 for 6–12 months and Phase II provides \$2M over 2 years and requires both research and development and commercialization plans. The Phase IIB Bridge Award supports technology validation and clinical translation, and Phase III, the commercialization phase, establishes a public-private partnership using non-SBIR/STTR funds.

The Bridge Award is issued as a milestone-based award to support commercialization for successful Phase II SBIR awardees. Since 2009, the NCI SBIR program has funded 28 Phase IIB awards, including 14 in devices and imaging; seven in therapeutics, and seven for *in vitro* diagnostics. To date, eight Bridge Award projects have been commercialized, and several others are moving through development. Strategic partners, venture capitalists, and state and local funders provide third-party matching funds. From 2009 to 2016, 21 Bridge Awards leveraged \$51M in NCI funding with \$220M in matching funds. A 2017 evaluation of the award period of the NCI SBIR Bridge Award program identified key strengths. The evaluation concluded that the program had successfully achieved its primary goal of leveraging NCI investments to accelerate the development and commercialization of SBIR-funded cancer technologies that may affect patient care. Proposed recommendations from the evaluation have informed the latest modifications to the program.

The reissue concept would support the continuation of promising cancer-focused SBIR Phase II projects, an increased budget limit of \$4M, and an expanded scope to include all technology areas within the NCI mission.

Subcommittee Review. Dr. Bhatia expressed the Subcommittee's strong support for the reissue concept. The Subcommittee noted the exceptional performance in turning NCI's \$51M investment into \$221M, an enviable metric. She informed members that the program is competitive, healthy, and impactful.

The first-year cost for the one-time re-issuance is estimated at \$12M for 5–40 R44 awards, with a total cost of \$60M for 3 years.

Questions and Answers

In response to a query from Dr. Wicha, Dr. Haim responded that discussions to incorporate the new tumor-infiltrating lymphocyte expansion technology into the CC are in progress. The company is actively working with the NCI and Dr. Steven Rosenberg. Those collaborations will be forthcoming.

Dr. Dafna Bar-Sagi, Vice Dean for Science, Senior Vice President, Chief Scientific Officer, Professor, Department of Biochemistry and Molecular Pharmacology and Medicine, New York Langone Medicine Center, New York University School of Medicine, asked about the success rate of other technologies, such as therapeutics. Dr. Haim explained that the timeline to commercialization is shorter for projects that are developing research tools. The funding requirement for therapeutics is higher, which affects their time to commercialization.

Motion. A motion to concur on the OD's reissue RFA entitled "SBIR Phase II Bridge Awards to Accelerate the Development of Cancer-Focused Technologies Toward Commercialization" was approved unanimously.

Division of Cancer Prevention

NCI Community Oncology Research Program (NCORP) (Re-Issue RFA) —Dr. Wortá McCaskill-Stevens

Dr. Wortá McCaskill-Stevens, Chief, Community Oncology and Prevention Trials Research Group, DCP, NCI, presented a reissue concept for the NCI Community Oncology Research Program, which was formed in 2014 to continue to provide access to cancer-related care for adults and children in their respective communities. The NCORP is composed of seven Research Bases (five NCI NCTN groups and two academic centers) and 46 Community Sites, 12 of which are Minority/Underserved (MU) Community Sites. The Community Sites reflect a significant diversity in institutional organizations and have engaged more than 4,000 investigators with access to more than 900 NCORP components. The broad portfolio of the NCORP network is focused in four areas: clinical trials for cancer control and prevention; accrual to NCTN treatment and imaging; cancer care delivery research (CCDR); and incorporation of cancer disparities research into clinical trials and CCDR.

From 2014 to 2016, NCORP enrolled nearly 18,000 patients into clinical trials. The overall minority enrollment was 21 percent, with 15 percent at Community Sites and 53 percent at MU Community Sites. Currently, 52 cancer control and prevention trials are active. Within the CCDR portfolio, two capacity assessments covering 225 practice units were completed. Of the five open studies, more than 1,300 patients have been accrued and seven protocols are in development. Collectively, the NCORP enrolled 41 percent of patients for the NCI-MATCH trial. Program evaluations and recommendations have informed the latest modifications to the program.

The reissue RFA would support the ongoing growth in existing research areas of the NCORP portfolio, resources and infrastructure for conducting clinical trials in the community setting, and a 22 percent increase in the budget that would be allocated over 6 years.

Subcommittee Review. Dr. Carol E. Ferrans, Professor and Associate Dean for Research Director, UIC Center of Excellence in Eliminating Health Disparities, Department of Biobehavioral Health Sciences, College of Nursing, University of Illinois Chicago, expressed the Subcommittee's strong enthusiasm for the concept reissuance. Dr. Ferrans informed members that the Subcommittee lauded the NCI for the success of the program in conducting clinical trials that span the spectrum of cancer control and treatment outcomes, as well as its inclusion of minority populations. The NCORP is addressing the

national priority to deliver effective cancer care to all communities, particularly those that are disadvantaged and difficult to reach geographically.

The first-year cost for the one-time re-issuance is estimated at \$149M for 61 awards, with a total cost of \$894M for 6 years.

Questions and Answers

Dr. Lacey suggested exploring opportunities to include incentives for payers and providers engaged in CCDR in the RFA.

Dr. Richard J. Thomas, Deputy Director, Office of Occupational Medicine, Occupational Safety and Health Administration, U.S. Department of Labor, asked about the return-to-work models for patients completing clinical care. Dr. Ann Geiger, Deputy Associate Director, Healthcare Delivery Research Program (HDRP), DCCPS, explained that they are actively working on initiatives to address return to employment and absenteeism among cancer survivors. Reports are expected to be released in 2018.

Motion. A motion to concur on the DCP's reissue RFA entitled "NCI Community Oncology Research Program" was approved unanimously.

Office of the Director

AIDS and Cancer Specimen Resource (ACSR) (Re-Issue RFA/Coop. Agr. – Limited Competition)—Dr. Rebecca Liddell Huppi

Dr. Huppi presented a reissue concept to support the activities of the ACSR, which aims to provide high-quality specimens from HIV-infected individuals with, or at substantial risk for, cancer at little or no cost to qualified investigators and to support biobanking for the AIDS Malignancy Consortium (AMC). The ACSR was established in 1993 and has maintained and grown an active program of creating tissue microarrays (TMAs) to conserve resources, while concomitantly increasing access to highly sought-after cancer specimens. The collection contains multiple cancer types, including KS, AIDS-related lymphoma, Hodgkin's disease, and anal and lung cancers. Special collections include specimens from clinical trials of the AMC, HIV multisite autopsy specimens, and several international collections.

The ACSR underwent a major restructuring to substantially enhance its function and utility. Changes included replacing four independently managed U01 awards with a single UM1 cooperative group; closing one underperforming biorepository, opening two domestic biorepositories, and opening one sub-Saharan Africa biorepository; and, developing and implementing the Annotation of a Tissue and Searching (ATLAS) platform. The current ACSR organizational structure is composed of five regional biospecimen repositories, a governing executive committee, a central operations and data coordinating center, and four working groups.

From 2013 to 2016, the ACSR disbursed more total specimens, created more TMAs, and disbursed more TMA cores than in the previous grant cycle. Tumor tissue distribution was 75 percent of the total samples procured in the same period. The ACSR has developed a series of special initiatives and special collections and maintains a biorepository to support the AIDS Malignancy Consortium. Key contributions to the field of HIV-associated malignancies include the development and early distribution of the BCBL1 cell line, which led to major contributions in KSHV research, and identification of prediagnosis biomarkers for AIDS-related non-Hodgkin lymphoma. Also, during the current grant cycle, ACSR published 42 manuscripts and 19 abstracts, representing one-third of the total publications of the 24-year history of the ACSR. In addition, 52 investigators in 35 separate institutions received specimens

from the ACSR. To date, the AMC biorepository serves more than 250 investigators in 25 domestic and seven sub-Saharan Africa sites. The Anal Cancer high-grade squamous intraepithelial lesions [HSIL] Outcomes Research (ANCHOR) biorepository, which the ACSR maintains, serves more than 50 research clinicians and scientists in 19 sites.

A 2016 mid-cycle program evaluation identified several strengths in support of concept reissuance and proposed recommendations that the ACSR began to rapidly address. This reissue concept also aligns with the 2017 recommendations of the BSA *ad hoc* Subcommittee on HIV and AIDS Malignancy.

The reissue RFA would support the ACSR's continuing to serve as the biorepository for the AMC and ANCHOR trials, enable investigators to conduct AIDS malignancy research using samples from LMICs, and maintain the existing repositories of specimens. The NCI-appropriated AIDS funds, as established by the OAR, will support this research.

Subcommittee Review. Dr. Emmons expressed the Subcommittee's support for the reissue concept and noted that it is a vital resource for very dedicated investigators. The Subcommittee recommends clarifying the strategic planning process and return on investment in the RFA.

The first-year cost for the one-time re-issuance is estimated at \$4.1M for years 1–2 and \$4.6M for years 3–5 for one UM1 award with a total cost of \$22M for 5 years.

Questions and Answers

Dr. Walker sought clarity on the number of investigators the ACSR serves. Dr. Huppi clarified that the ACSR disburses specimens for basic research and supports biorepository activities for the AMC in the United States and in sub-Saharan Africa. In this respect, it is serving 250 investigators.

Motion. A motion to concur on the OD's reissue and limited competition RFA/Coop. Agr. entitled "AIDS and Cancer Specimen Resource (ACSR)" was approved unanimously.

XI. SUBCOMMITTEE REPORTS—DR. ELIZABETH M. JAFFEE

NCAB *ad hoc* Subcommittee on Global Cancer Research. Dr. Ali-Osman provided a report of the 28 November 2017 meeting of the *ad hoc* Subcommittee on Global Cancer Research (GCR) and noted the success of the CGH. He noted that the Subcommittee heard about the mission and history of the CGH. Four main areas of focus were described and discussed at length: (1) the Global Pediatric Cancer Research effort to improve global pediatric Burkitt lymphoma research in LMICs and the establishment of the Burkitt Lymphoma Research Network; (2) programs to strengthen GCR at NCI-designated Cancer Centers; (3) CGH affordable cancer technology program; and, (4) non-NCI initiatives to increase availability of cancer drugs in Africa. The Subcommittee appreciated and is looking forward to NCI's establishing a Global Health Working Group.

Motion. A motion to accept the report of the 28 November 2017 NCAB *ad hoc* Global Cancer Research Subcommittee meeting was approved unanimously.

NCAB *ad hoc* Subcommittee on Population Science, Epidemiology, and Disparities. Dr. Paskett reported on the 28 November 2017 meeting of the *ad hoc* Subcommittee on Population Science, Epidemiology, and Disparities. Members reviewed and approved the draft charge and mission for the Subcommittee. Following was a discussion to establish a Working Group that would be separate

but complementary, undertaking all the background work and related research and making recommendations to the Subcommittee. The informed Subcommittee would make a report to the NCAB.

Members reviewed and approved a draft mission statement for the Working Group and identified key areas of focus: emphasizing better use of cooperative groups to address disparities in the near term; developing long-term goals for NCI's cohort portfolio; and undertaking a portfolio analysis for the science of survivorship and training activities.

Motion. A motion to accept the report of the 28 November 2017 NCAB *ad hoc* Population Science, Epidemiology, and Disparities Subcommittee meeting was approved unanimously.

BSA *ad hoc* Subcommittee on HIV and AIDS Malignancy. Dr. Robert Yarchoan, Director, OHAM, provided a report of the 21 June 2017 meeting of the *ad hoc* Subcommittee on HIV and AIDS Malignancy. The Subcommittee discussed the needs and priorities for HIV malignancy research at the NCI. Recommendations in eight specific areas were proposed, including KSHV-associated cancer; non-Hodgkin lymphoma, Hodgkin's disease, and Epstein-Barr virus-associated cancers; HPV-associated cancers; liver cancer; non-AIDS-defining cancers; addressing disparities in HIV-infected populations; international efforts; and general infrastructure. These recommendations will be further refined at the next meeting. The Subcommittee also discussed establishing working groups to focus on the immunologic aspects of therapies and vaccines for virus-induced malignancies and ways to enhance the research infrastructure for AIDS-associated malignancies. After discussion, members agreed to form one Working Group and drafted a proposed mission statement.

Motion. A motion to accept the report of the 21 June 2017 BSA *ad hoc* HIV and AIDS Malignancy Subcommittee meeting was approved unanimously.

XII. ONGOING AND NEW BUSINESS—DRS. CHI V. DANG AND ELIZABETH M. JAFFEE

Establishing BSA and NCAB Working Groups. Dr. Jaffee stated that the Boards will need to concur on establishing one BSA and four NCAB Working Groups. The goals, charges, and mission statements for each were provided in the Board book.

NCAB *ad hoc* Working Group on Informatics. Dr. Sharpless commented that the Working Group would be addressing a clear need for the NCI that also is an area on which the extramural community would like input.

Motion. A motion to concur with establishing an NCAB *ad hoc* Working Group on Informatics was approved unanimously.

NCAB *ad hoc* Working Group on Global Health.

Motion. A motion to concur with establishing an NCAB *ad hoc* Working Group on Global Health was approved unanimously.

NCAB *ad hoc* Working Group on SBIR/STTR.

Motion. A motion to concur with establishing an NCAB *ad hoc* Working Group on SBIR/STTR was approved unanimously.

NCAB *ad hoc* Working Group on Strategic Approaches and Opportunities in Population Science, Epidemiology, and Disparities.

Motion. A motion to concur with establishing an NCAB *ad hoc* Working Group on Strategic Approaches and Opportunities in Population Science, Epidemiology, and Disparities was approved unanimously.

BSA *ad hoc* Working Group on Immunology of Therapies and Vaccines and Research Structure.

Motion. A motion to concur with establishing an BSA *ad hoc* Working Group on Immunology of Therapies and Vaccines and Research Structure was approved unanimously.

XIII. NCAB CLOSED SESSION—DR. ELIZABETH M. JAFFEE

“This portion of the meeting was closed to the public in accordance with the provisions set forth in Sections 552b(c) (6), Title 5 U.S. code and 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. appendix 2).”

There was a review of intramural site visits and a discussion of personnel and proprietary issues. Members absented themselves from the meeting during discussions for which there was potential conflict of interest, real or apparent.

XIV. ADJOURNMENT—DRS. CHI V. DANG AND ELIZABETH M. JAFFEE

Dr. Jaffee thanked Board members, as well as all of the visitors and observers, for attending.

There being no further business, the 10th Joint Meeting of the BSA/NCAB was adjourned at 5:00 p.m. on Wednesday, 29 November 2017.

Date

Chi V. Dang, M.D., Ph.D., Chair, BSA

Date

Elizabeth M. Jaffee, M.D., Chair, NCAB

Date

Paulette S. Gray, Ph.D., Executive Secretary